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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,242	RUSSO ET AL.	
	Examiner	Art Unit	
	Gerald G. Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7,13 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *5,7,13 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibits A & B*.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed on 12/30/2004, in which claims 18 & 19 were amended. Claims 5-7, 13, 17-19 are pending and under consideration in the instant application.

Response to Amendment

Any rejection of record not addressed herein is withdrawn. With regard to the rejection of claims 5, 13 and 17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (i.e. for the incorporation of New Matter in the response filed on 7/16/2001), the rejection has been withdrawn in view of applicants' arguments. Specifically, the originally filed sequence listing for this application clearly demonstrates that the open reading frame encoding the TCL-1 protein described by SEQ ID NO: 2 extends from nucleotide 49 to nucleotide 387. Further, the specification clearly indicates that nucleic acids encoding a TCL-1 protein can be identified by nucleic acid hybridization under the stringent wash conditions recited in the claims using nucleic acids known to encode a TCL-1 protein (e.g. page 15, lines 1-24). The nucleic acid that is described in detail in the specification as encoding a TCL-1 protein is SEQ ID NO: 1. Therefore, applicants have implicit support for the added limitation, "that hybridizes under stringent conditions to a second nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387".

With regard to the rejection of claims 18 & 19 for lack of enablement, the amendment to the claims to include the limitation "whereby said isolated protein binds an antibody which also binds the TCL-1 protein of SEQ ID NO: 2" has overcome the rejection, but has also necessited

new grounds of rejection under 35 U.S.C. 112 1st paragraph for lack of sufficient written description to demonstrate possession of that which is now claimed (see below).

This action is not final as there are new grounds of rejection made herein that were not necessitated by applicants' amendment of the claims in the response filed on 12/30/2004.

Claim Objections

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6 is directed to an isolated TCL-1 protein comprising the amino acid sequence of SEQ ID NO: 2 from amino acid 1 to 113. Claim 7 is not directed to the protein of claim 6. Rather, claim 7 is directed to a "fragment of the protein of claim 6", which reads on proteins that are much smaller than the minimum size recited in claim 6. Therefore, claim 7 does not further limit claim 6.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As written, claim 7 is directed to a fragment of the protein of claim 6 (i.e. an isolated TCL-1 protein comprising the amino acid sequence of SEQ ID NO: 2 from amino acid 1 to 113). Since it is likely that fragments of the TCL-1 protein of claim 6 are

generated at various points during the life-cycle of T cells (e.g. during proteosome degradation, etc.), the claim reads on products of nature. It would be remedial to amend the claim by inserting the word "isolated" prior to the word "fragment".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 5, 13, 7 & 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new grounds of rejection.**

Claims 5, 13 and 17 are vague and indefinite in that the metes and bounds of the term "TCL-1 protein" are unclear as they are used in the claims. The specification does not clearly define the term TCL-1 protein in any limiting way. The specification does teach that a TCL-1 fragment may be a fragment or amino acid variant of the TCL-1 sequence shown in Figure 3a (i.e. SEQ ID NO: 2), so long as the fragment or amino acid variant is capable of displaying one of more biological activities associated with a full-length TCL-1 protein. According to the specification, such biological activities include but are not limited to antigenicity (i.e. the ability to bind to an anti-TCL-1 antibody) and immunogenicity (i.e. the ability to generate an antibody that is capable of binding a TCL-1 protein) (e.g. see page 9, line 35 to page 10, line 6). No other function is described for any TCL-1 protein. The designation "TCL-1" does not in and of itself necessarily convey any structural/functional information in the absence of a clear and limiting definition in the specification. Investigators routinely provide designations for genes and

proteins that may or may not have any correlation to a particular function for the gene or protein. In the instant case, the term "TCL-1" appears to be derived from a chromosomal breakpoint locus of more than 350 kb that can reasonably be expected to encode multiple different proteins having different functions. Since no other functional definition is provided in the originally filed specification for what constitutes a TCL-1 protein, it is unclear what is the minimal functional requirement for a protein to be considered a "TCL-1" protein? This rejection is not made against claims 6-7, as these claims are limited to the exemplified TCL-1 protein of SEQ ID NO: 2.

Claim 7 is vague and indefinite in that the metes and bounds of the term "specifically bound" are unclear. This subjective term is not explicitly defined in the instant specification, leaving it open to interpretation by the skilled artisan as to what degree of binding of other proteins by the antibody, or binding of other cross-reactive proteins by the recited protein fragment, is permitted such that the protein fragment still meets the limitation of being "specifically" bound.

Claim 17 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said nucleotide sequence" in part (b), line 2. For example, the recombinant expression vector of part (a) can reasonably be expected to comprise multiple, different sequences. It would be remedial to amend the claim by inserting the words "that encodes the TCL-1 protein" after the words, "said nucleotide sequence".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 & 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment of the claims in the response filed on 12/30/2004.**

Amended claim 7 is directed to a fragment of the protein described by SEQ ID NO: 2 which can be specifically bound by an antibody which also binds to the TCL-1 protein of SEQ ID NO: 2. Amended claims 18-19 are directed to isolated proteins comprising an amino acid sequence having at least 70% amino acid sequence identity to the amino acid sequence depicted in SEQ ID NO: 2, over a contiguous sequence of at least 25 or 50 amino acids, whereby said isolated protein binds an antibody that also binds to the TCL-1 protein of SEQ ID NO: 2. Applicants' response points to page 58, lines 16-24, for support for the newly added limitation "whereby said isolated protein binds an antibody that also binds to the TCL-1 protein of SEQ ID NO: 2". This citation does not, however, provide literal or implicit support for that which is now claimed. At best this citation provides support for generating antisera against the full-length protein described by SEQ ID NO: 2.

In the case of claim 7, the response does not point to where in the specification there is literal or implicit support for the recitation that the fragment of the protein of claim 6 necessarily binds to an antibody directed against the *particular* TCL-1 protein recited in claim 7 (i.e. the TCL-1 protein of SEQ ID NO: 2). While a convincing argument might be made that there is

implicit support for the newly added limitation for claim 7 (e.g. a reasoned argument citing the specification at page 9-line 25 to page 10-line 25), no such argument has been given to date. Until such a convincing argument is made of record, claim 7 is rejected for the reasons given above as comprising impermissible New Matter.

Even if such an implicit argument were accepted for claim 7, which is not guaranteed here, there does not appear to be implicit support for the limitation as it pertains to the broadly recited proteins of claims 18-19. For example, the teachings at pages 9-10 of the instant specification are all directed to TCL-1 protein fragments or variants whereas claims 18-19 are directed to *any* protein that meets the other functional limitations of the claims. Therefore, the teachings of the specification at pages 9-10 would not appear to provide support for claims 18-19 as currently written. Therefore, the newly added limitation to claims 18-19 is impermissible New Matter.

Finally, even if one were to accept that the limitation added to claims 18 & 19 is not new matter, it raises additional issues under 35 U.S.C. 112 1st paragraph with regard to written description. Claims 18-19 now claim a genus of proteins comprising a relatively limited percent identify (i.e. 70%) over a relatively short stretch of the TCL-1 protein described by SEQ ID NO: 2 which must meet the very specific functional limitation of being able to bind an antibody that also binds to the protein of SEQ ID NO: 2. The protein described by SEQ ID NO: 2 is 113 amino acid residues in length, meaning that a very large number of different possible variants and fragments of SEQ ID NO: 2 are encompassed by the rejected claims (e.g. every possible variant with up to 30% variance from SEQ ID NO: 2 over any possible fragment of SEQ ID NO: 2 of at least 25 or 50 residues in size).

The protein of SEQ ID NO: 2 was novel in the art at the time of filing. Neither the specification nor the prior art provide any teachings with regard to what are the antigenic epitopes within SEQ ID NO: 2 that are likely to generate antibodies with cross-reactivity to any other particular protein that comprises only 70% identity over a relatively short fragment of SEQ ID NO: 2. The specification and prior art thus provide no basis for the skilled artisan to envision which of the many possible variants of SEQ ID NO: 2 will necessarily cross-react with an antibody that binds to the protein of SEQ ID NO: 2. Because of this lack of a structural/functional correlation between the protein variants which are encompassed by the claim and the recited functional limitation, the skilled artisan would not have been able to envision a sufficient number of specific embodiments of the recited proteins to describe the broadly claimed genus of proteins that actually do retain the ability to cross-react with an antibody that binds the protein of SEQ ID NO: 2. Therefore, the skilled artisan would reasonably have concluded applicants were not in possession of the broadly claimed genus of proteins.

Claim 7 is not rejected on these grounds. Claim 7 is limited to fragments of the protein of SEQ ID NO: 7. Even though it is recognized that not all of the possible fragments of the protein of SEQ ID NO: 2 would be bound by the recited antibody against the protein of SEQ ID NO: 2, it is expected that a significant number of these fragments would necessarily bind the recited antibody under at least some conditions, and applicants have clearly demonstrated that they are in possession of the protein of SEQ ID NO: 2 as well as its fragments.

Claims 5 & 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated proteins that bind to an antibody that binds to the TCL-1 protein of SEQ ID NO: 2, does not reasonably provide enablement for isolated protein that are not bound by an antibody that binds to the TCL-1 protein of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **This is a new rejection.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Breadth of the claims: Claim 5 is directed to an isolated TCL-1 protein comprising an amino acid sequence encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). Claim 5 reads on a protein that comprises only a short peptide sequence with sufficient identity to a portion of SEQ ID NO: 2 that its coding sequence would retain sufficient homology to the corresponding coding sequence within SEQ ID NO: 1 such that hybridization to the complement of SEQ ID NO: 1 could occur under the recited wash conditions.

Claim 13 is directed to a fusion protein comprising a TCL-1 protein sequence of at least 10 amino acids linked to a non-TCL protein sequence, wherein the TCL-1 protein sequence is encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). There is no limitation that the 10 amino acid residues are 10 contiguous amino acid residues from SEQ ID NO: 2, only that they are from a "TCL-1" protein.

The prior art teaches that the optimum-sized peptide for generating antisera is from 10-20 amino acid residues in length, although peptides as small as 8 residues in length may be used to generate antisera (see page 71, section 1.1.3 in Hancock, et al. "Synthesis of Peptides for Use as Immunogens", Methods in Molecular Biology, Vol. 80: Immunochemical Protocols, 2nd edition. J.D. Pound, editor, pages 69-79, Humana Press). Further, because of the degeneracy of the genetic code, it is not required that the 8-10 residues have perfect identity to SEQ ID NO: 2 for the corresponding nucleic acid sequence to have sufficient homology to the corresponding sequence from SEQ ID NO: 1 in order for it to remain hybridized under the recited wash conditions. For example, a leucine substitution for isoleucine would be considered a conservative substitution at the amino acid level and would encompass several possible overlapping codons that differ minimally (e.g. CUA, CUU, CUC, CUG for leucine; AUA, AUU, AUC for isoleucine). Such conservative substitutions from the sequence of the protein of SEQ ID NO: 2 might then have very little effect on the degree of homology between the corresponding nucleic acid sequence and the recited open reading frame from SEQ ID NO: 2. For example, the MTCP-1 protein (Accession No. P5678) described by Fu et al (Proceedings of

the National Academy of Sciences, USA. 1998, Vol. 95, pages 3413-3418) comprises a sequence of 10 amino acids with 80% identity to amino acid residues 71-80 of SEQ ID NO: 2 (see the attached sequence search results in Exhibit A). According to the genetic code, one can encode for this region of the MTCP protein with a synthetic oligonucleotide that has 28/30 nucleotides along its length to the corresponding region of SEQ ID NO: 1. One of skill in the art would necessarily expect that such an oligonucleotide would remain hybridized to the recited complementary sequence of SEQ ID NO: 1 under the recited conditions for at least some period of time. It is noted that, even though there is a region within the MTCP-1 polypeptide that meets the recited structural limitations of the claims, the overall identity of the MTCP-1 protein to the TCL-1 protein of SEQ ID NO: 2 is only ~36%. Thus, a protein with only limited homology to the TCL-1 protein of SEQ ID NO: 2 can still satisfy the recited claim limitations.

Further, there is no limitation in the rejected claims that the first nucleic acid sequence is present in the context of the larger nucleic acid sequence during the hybridization conditions. Nor is there any limitation with regard to the duration for the wash step recited in the rejected claims. For at least the reasons given above, the claimed proteins need only comprise a relatively small number of amino acid residues with less than complete identity to SEQ ID NO: 2. Thus, claims 5 & 13 encompass a very large number of different protein sequences.

Guidance of the specification/The existence of working examples: The specification does not clearly define what constitutes a "TCL-1" protein for proteins other than the exemplified embodiment depicted by SEQ ID NO: 2. The specification does teach that a TCL-1 fragment may be a fragment or amino acid variant of the TCL-1 sequence shown in Figure 3a (i.e. SEQ ID NO: 2), so long as the fragment or amino acid variant is capable of displaying one of more

biological activities associated with a full-length TCL-1 protein. According to the specification, such biological activities include *but are not limited to* antigenicity (i.e. the ability to bind to an anti-TCL-1 antibody) and immunogenicity (i.e. the ability to generate an antibody that is capable of binding a TCL-1 protein) (e.g. see page 9, line 35 to page 10, line 6). No other function is described for any TCL-1 protein. Further, the instant specification provides no teaching as to what other functional "TCL-1" proteins might be found from different sources (e.g. allelic variants, variants from different species, etc.).

The specification does teach that the gene encoding the TCL-1 protein of SEQ ID NO: 2 has been identified as being involved in chromosomal translocation events correlated with several post-thymic types of T cell leukemias and lymphomas (e.g. page 2, lines 13-23 of the instant specification). The only asserted utility for the TCL-1 proteins of the invention is for generating antisera that is capable of binding to TCL-1 and which might be useful in the diagnosis and/or treatment of different post-thymic T cell disorders (e.g.. pages 32-32, bridging paragraphs).

Nature of the invention: The nature of the invention is complex in that it involves the use of a protein whose basic biological function was not known at the time of the invention beyond the observation that the gene encoding the protein has been identified as being involved in chromosomal translocation correlated with several post-thymic types of T cell leukemias and lymphomas (e.g. page 2, lines 13-23 of the instant specification).

State of the art: The TCL-1 protein described by SEQ ID NO: 2 was novel in the art at the time of the invention. Thus, the prior art does not offset the deficiencies of the instant

specification with regard to how one would make and use the recited proteins if they are not effective in generating an antibody that is capable of binding SEQ ID NO: 2.

Predictability of the art/The amount of experimentation necessary: Given the combination of factors outlined above, in particular the very limited teachings of the instant specification with regard to how one would use the recited proteins that do not bind to an antibody that also binds to the TCL-1 protein of SEQ ID NO:2, it would have required undue, unpredictable experimentation of an inventive nature to make and use the claimed proteins in the full, broad scope currently recited in the rejected claims.

Claims 5, 13 & 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Claim 5 is directed to an isolated TCL-1 protein comprising an amino acid sequence encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). Claim 5 reads on a protein that comprises only a short peptide sequence with sufficient identity to a portion of SEQ ID NO: 2 that its coding sequence would retain sufficient homology to the corresponding coding sequence within SEQ ID NO: 1 such that

hybridization to the complement of SEQ ID NO: 1 could occur under the recited wash conditions.

Claim 13 is directed to a fusion protein comprising a TCL-1 protein sequence of at least 10 amino acids linked to a non-TCL protein sequence, wherein the TCL-1 protein sequence is encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). There is no limitation that the 10 amino acid residues are 10 contiguous amino acid residues from SEQ ID NO: 2, only that they are from a "TCL-1" protein.

Claim 17 is directed to a method of producing a recombinant TCL-1 protein comprising culturing a host cell transformed with a recombinant expression vector comprising a nucleotide sequence that encodes a TCL-1 protein such that the TCL-1 protein is expressed by the cell and recovering the protein. The claim specifies that a first nucleic acid molecule consisting of the nucleic acid sequence encoding the TCL-1 protein hybridizes under specifically recited stringency conditions to a second nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). The term TCL-1 protein is not explicitly defined in the instant specification and can be interpreted as encompassing less than full length proteins obtained from any "TCL-1" protein.

The prior art teaches that the optimum-sized peptide for generating antisera is from 10-20 amino acid residues in length, although peptides as small as 8 residues in length may be used to generate antisera (see page 71, section 1.1.3 in Hancock, et al. "Synthesis of Peptides for Use as

Immunogens", Methods in Molecular Biology, Vol. 80: Immunochemical Protocols, 2nd edition. J.D. Pound, editor, pages 69-79, Humana Press). Further, because of the degeneracy of the genetic code, it is not required that the 8-10 residues have perfect identity to SEQ ID NO: 2 for the corresponding nucleic acid sequence to have sufficient homology to the corresponding sequence from SEQ ID NO: 1 in order for it to remain hybridized to the complement of SEQ ID NO: 1 under the recited wash conditions. For example, a leucine substitution for isoleucine would be considered a conservative substitution at the amino acid level and would comprise several possible overlapping codons that differ minimally (e.g. CUA, CUU, CUC, CUG for leucine; AUA, AUU, AUC for isoleucine). Such conservative substitutions from the sequence of the protein of SEQ ID NO: 2 might then have very little effect on the degree of homology between the corresponding nucleic acid sequence and the recited open reading frame from SEQ ID NO: 2. For example, the MTCP-1 protein (Accession No. P5678) described by Fu et al (Proceedings of the National Academy of Sciences, USA. 1998, Vol. 95, pages 3413-3418) comprises a sequence of 10 amino acids with 80% identity to amino acid residues 71-80 of SEQ ID NO: 2 (see the attached sequence search results in Exhibit A). According to the genetic code, one can encode for this region of the MTCP protein with a synthetic oligonucleotide that has 28/30 nucleotides along its length to the corresponding region of SEQ ID NO: 1. One of skill in the art would necessarily expect that such an oligonucleotide would remain hybridized to the recited complementary sequence of SEQ ID NO: 1 under the recited conditions for at least some period of time. It is noted that, even though there is a region within the MTCP-1 polypeptide that meets the recited structural limitations of the claims, the overall identity of the MTCP-1

protein to the TCL-1 protein of SEQ ID NO: 2 is only ~36%. Thus, a protein with only limited homology to the TCL-1 protein of SEQ ID NO: 2 can still satisfy the recited claim limitations.

Further, there is no limitation in the rejected claims that the first nucleic acid sequence is present in the context of the larger nucleic acid sequence during the hybridization conditions. Nor is there any limitation with regard to duration for the wash step recited in the rejected claims. For at least the reasons given above, the claimed proteins need only comprise a relatively small number of amino acid residues with less than complete identity to SEQ ID NO: 2. Thus, claims 5, 13 & 17 encompass a very large genus of different proteins.

The TCL-1 protein of SEQ ID NO: 2 appears to have been novel in the art at the time of filing and no other TCL-1 protein appears to have been described in the prior art at that time. Thus, there is no basis in the prior art or originally filed specification for one of skill in the art to envision a sufficient number of representative embodiments of the recited "TCL-1" proteins to describe the broadly claimed genus of such proteins that meet the structural requirements of the rejected claims. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the broadly claimed genus of "TCL-1" proteins.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 5 is directed to an isolated TCL-1 protein comprising an amino acid sequence encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). Claim 5 reads on a protein that comprises only a short peptide sequence with sufficient identity to a portion of SEQ ID NO: 2 that its coding sequence would retain sufficient homology to the corresponding coding sequence within SEQ ID NO: 1 such that hybridization of the two nucleotide sequences could occur under the recited wash conditions.

Amended claim 7 is directed to a fragment of the protein described by SEQ ID NO: 2 which can be specifically bound by an antibody which also binds to the TCL-1 protein of SEQ ID NO: 2. There is no limitation that the fragment is in any particular context (e.g. isolated from surround amino acid sequences with which it is normally associated).

Claim 13 is directed to a fusion protein comprising a TCL-1 protein sequence of at least 10 amino acids linked to a non-TCL protein sequence, wherein the TCL-1 protein sequence is encoded by a first nucleic acid that hybridizes under specifically recited stringency conditions to

a nucleic acid that consists of the complement of the nucleotide sequence of SEQ ID NO: 1 from nucleotide 49 to nucleotide 387 (i.e. the open reading frame for the TCL-1 protein of SEQ ID NO: 2 as shown in Figure 3a). There is no limitation that the 10 amino acid residues are 10 contiguous amino acid residues from SEQ ID NO: 2, only that they are from a "TCL-1" protein.

Claims 5, 7 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern, et al (Oncogene, September 1993, Vol. 8, No. 9, pages 2475-2483; see the entire reference). **This is a new rejection.**

Stern et al teach the characterization of a gene encoding a novel protein, mature T cell proliferation-1 protein (MTCP-1) and provide a predicted amino acid sequence based upon the identified open reading frame (e.g. Figure 5c; Accession No. S78532). Stern et al teach that the gene encoding MTCP-1 is translocated from human chromosome Xq28 to the alpha/delta locus in mature T cell proliferations (e.g. Abstract).

The MTCP-1 protein described by Stern et al comprises a sequence of 10 amino acids with 80% identity to amino acid residues 71-80 of SEQ ID NO: 2 (see the attached sequence search results in Exhibit B). Using the corresponding nucleotide sequence of SEQ ID NO: 1 (i.e. CTG CCT **A**TC ATG TGG CAG CTC TAC CCT GA**T**), and considering the genetic code, one of skill in the art can generate a synthetic oligomer of 30 polynucleotides in length that encodes the corresponding amino acid sequence from MTCP-1 taught by Stern et al and which comprises two nucleotide substitutions relative to the sequence from SEQ ID NO: 1 (underlined and in bold above). Such an oligomer would have a dissociation temperature of ~82°C in 0.9 M NaCl based upon the formula:

$T_d(°C) = 4(G + C) + 2(A + T)$
$T_d(°C) = 4(16) + 2(14)$
$T_d(°C) = 64 + 28$
$T_d(°C) = 92°C - (2 X 5°C/mismatch) = \sim 82°C$

(Wahl, et al. Molecular Hybridization of Immobilized Nucleic Acids: Theoretical Concepts and Practical Considerations, in Methods in Enzymology: Guide to Molecular Cloning; Berger & Kimmel, editors; Vol. 152, pages 399-407; 1987)

Granted that the cation concentrations recited in the rejected claims are considerably lower than 0.9 M NaCl, one of skill in the art would still necessarily expect that at least a portion of a mixture of such 30-mers directed against the corresponding sequence from the complement of SEQ ID NO: 1 would remain hybridized under the recited wash conditions. It is again noted that there is no recitation for duration of the wash step in the rejected claims. Hence, the protein sequence taught by Stern et al meets the limitations of the rejected claims with regard to the sequence that encodes it.

Stern et al do not actually isolate or produce the MTCP-1 protein.

It would have been obvious to one of ordinary skill in the art at the time of the invention to construct an expression vector encoding the predicted amino acid sequence for MTCP-1 and to recombinantly produce the predicted polypeptide. One would have been motivated to do so in order to receive the expected benefit of being able to further characterize the biochemical and functional activities of a novel protein that appears to be expressed in several important human disorders (e.g. by preparing antibodies against the protein to determine when the protein is expressed in T cells). Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing the deduced amino acid sequence taught by Stern et al to recombinantly produce the MTCP-1 protein and characterize it's role in T cell proliferative disorders.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

Claim 6 is allowed. Claims 5, 7, 13 & 17 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G. Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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